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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/522,208

10/27/2005

Mezher Hussein Ali

AC-21-US

3691

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75 MAIN STREET , SUITE 301  
MILLBURN, NJ 07041

EXAMINER

CHANG, CELIA C

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

12/11/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/522,208	<b>Applicant(s)</b> ALI ET AL.	
	<b>Examiner</b> Celia Chang	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13-30 is/are pending in the application.
- 4a) Of the above claim(s) 15-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Applicant's election with traverse of group I, species of example 11 on Aug. 29, 2008 is acknowledged. The traversal is on the ground that the international search was made without serious burden. Please note that the 371 document submitted on 1/13/2005 clearly stated that claims 1-30 were searched and examined *in part*. Therefore, the entire application was not searched.

Further, the restriction in national stage is proper according to the PCT rules and 37 CFR 1.499. According to PCT Rule 13.1 Annex B, **Part 1(f)v**, indicates that

*"When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the examiner"*

The anticipatory compounds were clearly pointed out in US 4,639,436. Therefore, the lacking of unity has been found.

The requirement is still deemed proper and is therefore made FINAL.

Claim 12 has been canceled. Claims 3-6, 11 and claims 1-2, 7-10, 13-14 reading on formula I wherein R is C<sub>1-3</sub>AlkylAr<sup>1</sup> and Ar<sup>1</sup> is substituted phenyl is prosecuted. Claims 15-30 and the remaining subject matter of claims 1-2, 7-10, 13-14 are withdrawn from consideration per 37 CFR 1.142(b).

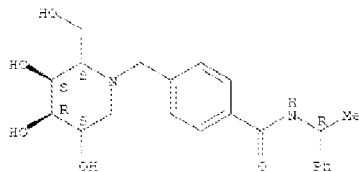
2. Claims 1-10, 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims used "..." or "◀" in the structural formula. It is well recognized in the chemical art that stereo-limitations are defined by the "S" or "R" configuration at a chiral center. The "..." or "◀" notation is not stereo limitation but up and down from the ring. Because six membered ring systems have axial orientation, the up and down arrows do not offer any stereo-limitation. See for example the following structures recited by CAS:

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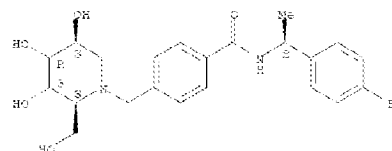
RN 644960-55-4 CAPLUS  
 CN Benzamide, N-[(1R)-1-phenylethyl]-4-[(1S,3S,4R,5R)-3,4,5-trihydroxy-2-(hydroxymethyl)-1-piperidinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 644960-54-3 CAPLUS  
 CN Benzamide, N-[(1S)-1-(4-fluorophenyl)ethyl]-4-[(1S,3S,4R,5R)-3,4,5-trihydroxy-2-(hydroxymethyl)-1-piperidinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



Stereo-limitation is properly made as seen in the above CAS delineation that the proper “R” or “S” notation at each chiral center must be placed.

The following rejections of 102 or 103(a) are made based on none stereo limited formula I as claimed.

3. Claims 1-11, 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The term “prodrug” was not defined or what kind of prodrug was disclosed in the specification. It is well recognized that prodrug is an unpredictable preparation of the lead compound wherein the "prodrug" is inactive and depend solely on the activity being release in vivo of the lead compound. Nowhere in the specification provided sufficient information as to what kind of modification of the drug functional groups as to result in an inactive prodrug which will be released into the active form in vivo.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Boeshagen et al. CA 113:126581, see RN attached; Ezure et al. CA 116:236093, RN 141206-38-4; Broek et al. Ca 119:96007, RN 149302-52-3, RN 149302-53-4; Berg et al. RN 8117-43-3; Kurihara et al. CA 114:185939 RN 133342-47-9; when the “...” or “◀” of the formula placed no limitation for the “R” or “S” configuration of the chiral center. The Boeshagen, Broek, Berg and Kurishara anticipated even the “...” or “◀” features of the claims.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

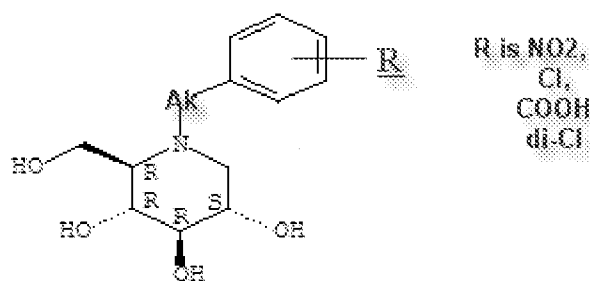
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boshagen et al. US 5,051,407.

Determination of the scope and content of the prior art ( MPEP §2141.01)

Boshagen et al. ‘407 disclosed anticipatory compounds which has been delineated supra (see CA113:126581). The patent further disclosed structurally analogous species as found at col. 10, lines 10-11, 6-28, 33). The compounds basically have the structure as:

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And many other compounds when the Ak linker contains an oxygen with a varieties of substituents including cyano, amino, amido etc. as claimed (see compounds at col.8-11).

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

The difference between the above exemplified species and the instant claims is that the substituents R of the above formula wherein the prior art exemplified halogen, amino or dihalogen etc. the instant claims are limited to cyano, CON(R<sup>1</sup>)<sub>2</sub>,..... etc. (see claim 1). Generically, the Boshagen et al. '407 disclosed that substituents on the aryl moiety can be 1-3 independently selected from nitro, cyano, amino, aminosulfonyl, alkylcarbonylamino etc. (see col. 4 lines 4-43) with exemplification with Ak linker having a CH<sub>2</sub> replaced by O,S or N (see CA113 delineation).

*Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)*

One having ordinary skill in the art in possession of the generic teaching and multiple examples of Boshagen et al. '407 would be in possession of the prior art disclosed compounds which encompassed the instant claims. The difference between the prior art species and the instant claimed species are the mere picking and choosing among the many alternative choices of substituents which have been clearly delineated and exemplified by the prior art. In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814, especially, the prior art is well exemplified with multiple variations including multiple substitutions.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacob US 6,225,325 in view of Greene.

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Jacob '325 generically disclosed 1,5-dideoxy-1,5-imino glucitol or galactiol compounds which inhibits glucosylceramide synthesis (see col. 1-2, especially paragraph bridging). Examples were disclosed wherein the instant Ar1 is unsubstituted or methylsubstituted (see col. 8 lines 65-66,, col. 9, lines 1-2).

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

The difference between the prior art compounds and the instantly claimed/elected species is that instead of benzyloxy, the prior art compounds have a methyl substitution. Generically, Jacob '325 taught that the protected hydroxy substitution is an alternative choice for the exemplified methyl (see col. 7, lines 8-10). Greene reference provided evidence that protected hydroxy includes benzyl protection (see p.10,11, 29), i.e. a benzyloxy moiety.

*Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)*

One having ordinary skill in the art in possession of the Jacob. '325 is in possession of the instantly claimed/elected species because one having ordinary skill in the art would expect all the generic teaching of the reference to be operable. The modification of an exemplified compound with an alternative choice of substituent is prima facie obvious. In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

7. Claims 1-11, 13-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 13-14 of copending Application No. 10/522,207 or 10/586,188 in view of US 5,051,407, US 7,256,005 and Kato et al.

The difference between the copending claims and the instant claims is the stereo-arrangement of the hydroxymethyl and the triol groups. US 5,051,407 and US 7,256,005 taught that variation of stereo structure of the piperidine core would not affect the activity and are alternative choices for such compounds (see especially, '005 col. 7-8) and Kato et al. disclosed the same expectation that all enantiomers are biologically active while some may be more active or selective than others against specific enzymes and provided routine synthesis for such compounds. The knowledge that enantiomers are all active but with different degree of activity would have motivated one having ordinary skill to prepare all enantiomers with the expectation that all compounds are active and some may be better than others. In absence of unexpected results, preparation of stereo-isomer among the copending claims is prima facie obvious.

This is a provisional obviousness-type double patenting rejection.

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The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang  
Dec. 3, 2008

/Celia Chang/  
Primary Examiner  
Art Unit 1625